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EFFECTS OF TESTOSTERONE SUPPLEMENT THERAPY ON CARDIOVASCULAR OUTCOMES IN MEN WITH LOW TESTOSTERONE

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Background: Cardiovascular (CV) effects of testosterone supplement therapy in men with low testosterone levels have been inconsistently documented across studies.

Methods: Data for men with low total testosterone levels (<300 ng/dL) during 2007-13 were obtained from a large community-based healthcare system. Cox proportional hazards (CPH) models were developed to examine effects of testosterone therapy on CV outcomes (acute myocardial infarction [AMI], stroke or death). Single- and multi-variable models and stepwise-variable selection procedures provided estimates of unadjusted and adjusted hazard ratios (HR) and identified best predictors of outcome. Adjusted effects of testosterone supplement were also examined in a subset of patients 1:1 propensity-matched (caliper=0.10) by several variables.

Results: A total of 7,245 men were identified, with a mean age of 54 yrs and mean follow-up period of 1.78 yrs (SD=0.86). Dyslipidemia was present in 41%, hypertension in 34%, current or prior smoking in 25%, diabetes mellitus in 17% and chronic kidney disease in 3.4%. The combined event rate of AMI, stroke and death at 3 years was low in the treated (5.5%) and untreated (6.7%) groups. On single-variable CPH analysis, testosterone therapy appeared to be beneficial with reduced outcomes [unadjusted HR: 0.71 (0.51-0.98); p=0.038]. However, on multi-variable analysis, after adjusting for baseline differences, testosterone therapy was no longer significant (p=0.54). Age, prior AMI and stroke/transient ischemic attack, dyslipidemia, smoking status and length of follow-up were independent predictors of the combined outcome. Effects of testosterone supplement on CV outcomes were non-significant when adjusted through 1:1 matching in 3,115 matched-pairs [adjusted HR: 0.86 (0.57-1.29)] and the mean number of days to a CV event [1,044 (SE=4) vs. 955 (SE=3)] did not differ between treated and non-treated men (P=0.46).

Conclusion: CV event rates were low in men with low testosterone. While unadjusted analysis suggests CV benefits of testosterone replacement, men treated vs. not treated for low testosterone differ in CV risk factors and, when accounted for, differences in CV outcomes disappear.